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FORMULATION AND EVALUATION OF GASTRO-RETENTIVE DRUG DELIVERY SYSTEM OF ATORVASTATIN CALCIUM

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ABSTRACT

Atorvastain is a HMG-CoA reductase inhibitor used in the treatment of hyperlipidaemia. The absolute bioavailability of atorvastatin is approximately 14%. It also undergoes high first pass metabolism. Here, an attempt is made to formulate gastro-retentive non-effervescent floating tablets of atorvastatin to prolong the residence time of the dosage forms within the GIT. Atorvastatin showed wavelength maxima at 243 nm in 0.1 N HCL + 0.5% SLS. Various formulations were developed by using release rate controlling HPMC K4M, HPMC E5LV and POLYOX 303 in combinations by direct compression method. The prepared tablets were characteristics by good hardness, weight variation, friability, lag time, total floating time, in vitro drug release using USP dissolution test apparatus Type – II (paddle method) in dissolution medium of 0.1 N HCl + 0.5% SLS. Drug-polymer compatibility studies by FTIR gave conformation about drug purity and showed no interaction between drug and selected polymers. From among all the developed formulations, as F_2 prolonged the drug release (98.73±0.62 %) for longer period of time (24 hrs.); The lag time of optimized formulation (F_2) was upto 116 sec. they were selected as optimized formulations. The optimized formulations were found to be stable during stability studies for one month.

KEYWORDS: Atorvastatin Calcium, Non-Effervescent Floating Drug Delivery System, Stability Study & In-Vitro Drug Release

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Original Article

INTRODUCTION

Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. Gastro-retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug wastage, and improves solubility for drugs that are less soluble in a high pH environment.

GRDF extend significantly the duration of time over which the drugs may be released. They not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage form.

Conventional oral controlled dosage forms suffer from mainly two adversities. The short gastric retention time (GRT) and unpredictable gastric emptying time (GET), so GRT and GET are important considerations to formulate a controlled release dosage form having required extended GI residence time.

A number of approaches have been used to increase the GRT of a dosage form in stomach by employing a variety of concepts. These include – Single-unit dosage forms like Floating Systems, High Density Systems, Bio/Muco-adhesive Systems, Swelling and Expanding Systems, Incorporation of Passage Delaying Food Agents,

Ion-Exchange Resins, Osmotic Regulated Systems, pH-Independent formulation, Fluid filled floating chamber, and Multiple-unit dosage forms.

The floating drug delivery system (FDDS) also called Hydrodynamically Balanced Drug Delivery System (HBS). FDDS is an oral dosage forms (capsule or tablet) designed to prolong the residence time of the dosage form within the GIT. It is a formulation of a drug with gel forming hydrocolloids meant to remain buoyant on stomach contents. Drug dissolution and release from dosage retained in the stomach fluids occur at the pH of the stomach under fairly controlled condition.

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS, which are Effervescent System and Non- Effervescent System.

The Non-effervescent FDDS is based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, hydrophilic gums, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bioadhesive polymer such as Chitosan and Carbopol.

MATERIALS AND METHODS

MATERIALS

Atorvastatin calcium was received from Alembic pharma, vadodara, HPMC (hydroxyl-propyl methylcellulose) K4M, HPMC E5LV, Polyox 303, Lactose, PVP, Mg. Stearate, Talc, from Yarrow chem. Ltd, Mumbai.

METHODS

Pre-Compression Properties

Direct compression is defined as a process by which tablets are compressed directly from powder blends of the active ingredients and suitable excipients, Before employing direct compression as a method of preparation of tablets, the powder properties of the ingredients should be assessed to ascertain their stability for direct compression. The powder of polymer and drugs were characterized by angle of repose, bulk density, tapped density, % compressibility, and hausner ratio. The flow properties of powders have a great impact on tableting because it requires the flow of materials from a storage container to filling stations.

- **Angle of Repose**

The frictional forces in a loose powder can be measured by the angle of repose (ϕ). It is an indicative of the flow properties of the powder. It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane. Angle of repose was determined by using funnel method. Powder was poured from funnel, which can be raised vertically until a maximum cone height.

$\tan \phi = 2h/D$ or $[\phi = \tan\text{-}1\ (2h/D)]$

Where, h was obtained Height. D was Diameter of heap.

- **Bulk Density (Db)**

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve #20) into a measuring cylinder and the initial volume was noted. From this, the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by:

Db = M / V0

Where, M is the mass of powder, V0 is the bulk volume of the powder.

- **Tapped Density (Dt)**

It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted, if the difference between these two volumes is less than 2% then stopped tapping. And if it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2%. It is given by:

Dt = M / Vt

Where, M is the mass of powder, Vt is the tapped volume of the powder.

- **Compressibility Index (Carr's Consolidation Index)**

One of the ways of measurement of free flowing powder is compressibility as computed from density of a powder. It was calculated by using the formula

% Compressibility = [Tapped density-Bulk density/Tapped density] x 100

- **Hausner Ratio**

Hausner ratio is an indirect index of ease of powder flow. If the hausner ratio of powder is near to 1.25, indicates better powder flow. It is calculated by the formula

Hausner Ratio = Dt / Db

Where, Db = Bulk density of the powder Dt = Tapped density of the powder.

PREPARATION OF FLOATING TABLETS

Each tablet containing 60 mg of Atorvastatin calcium was prepared by direct compression method. Polymers HPMC K4M, HPMC E5LC, POLYOX 303 was used in the different concentration. All the ingredients were passed through sieve 100# and then geometrical mixing of all the ingredients were done except magnesium stearate and talc. They were added at the end. The mixed blend of drug and the excipients was compressed using RIMEK 10 station rotary punching machine to produce tablet weighing 200 mg.

EXPERIMENTAL DESIGN

Plackett-Burman factorial design was applied. This designs can identify main factors from the large number of suspected contributor factors for the desired response variables. Therefore, these designs are extremely useful in preliminary studies where the aim is to identify formulation variables that can be fixed or eliminated in further

investigation. The model is of the form:

$$Y= \beta_0 + \beta_1X_1 + \beta_2X_2 + \beta_3X_3 + \beta_4X_4 + \ldots\ldots\ldots\ldots \beta_nX_n$$

Where Y is the response, β_0 is a constant and β_1 to β_n are the coefficients of the response values.

EVALUATION OF FLOATING TABLETS OF ATORVASTATIN CALCIUM

General Appearance and Organoleptic Properties

The control of a general appearance of a tablet involves the measurement of a number of attributes such as a tablet's size, shape, color, presence or absence of an odor.

Hardness

Hardness (diametric crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The hardness was tested using Monsanto tester. Hardness factor, the average of the six determinations, was determined and reported. The force was measured in kilograms per centimeter square.

Friability

Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. Permitted friability limit is 1.0 %. 20 tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets were exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. It was rotated at a rate of 25 rpm. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively. The percent friability was determined using the following formula;

$$\text{Friability} = \frac{(W1-W2)\ X\ 100}{W1}$$

Where, W1 = weight of the tablet before test, W2= weight of the tablets after test

Weight Variation

Twenty tablets were weighed individually and all together. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the permissible limits (±7.5%) as per IP. The percent deviation was calculated using the following formula.

$$\text{Percentage Deviation} = \frac{\text{Individual weight} - \text{Average weight}\ X\ 100}{\text{Average weight}}$$

Floating Lag Time and Total Floating Time

The media was 900ml of 0.1 N HCL (pH 1.2) taken in a beaker and the temperature was maintained to 37 + 0.50 ^{0}C throughout the study. The buoyancy lag time and total floating time was calculated. Buoyancy lag time was calculated with Digital Stop Watch and total floating time was calculated visually.

Dissolution Studies

The study was carried out using dissolution apparatus USP Type II (Paddle). Dissolution medium was 900 ml 0.1 N HCL. Speed of paddle was 50 rpm. Temperature of medium was 37 + 0.5 ^{0}C. Aliquot 5 ml was collected from solution every 1 hr for up to 24 hrs, filtered through Whatmann Filter Paper no. 41 and absorbance was recorded at 243nm.

Details of Dissolution Test

- Apparatus : USP Type II
- Volume of medium : 900 ml
- Temperature : 37 ± 0.5 $^\circ$C
- Paddle Speed : 50 rpm
- Dissolution medium used : 0.1 N HCl + 0.5% SLS
- Aliquot taken at each time interval : 5 ml

Stability Study

Stability studies were conducted on the optimized tablet batches F_2 to assess their stability after storage. They were packed in aluminum foil and stored under the storage conditions of 40°C ± 2°C Temp. and 75% ± 5% RH for a period as prescribed by ICH guidelines.

Table 1: Plackett-Burman Design in Coded Form

RUN	HPMC K4M	HPMC E5LV	LACTOSE	POLYOX 303	PVP	Mg. STEARATE	TALC
F_1	+1	+1	+1	-1	+1	-1	-1
F_2	-1	+1	+1	+1	-1	+1	-1
F_3	-1	-1	+1	+1	+1	-1	+1
F_4	+1	-1	-1	+1	+1	+1	-1
F_5	-1	+1	-1	-1	+1	+1	+1
F_6	+1	-1	+1	-1	-1	+1	+1
F_7	+1	+1	-1	+1	-1	-1	+1
F_8	-1	-1	-1	-1	-1	-1	-1

Table 2: Formulation of Non-Effervescent Floating Tablet Batches F1-F8 by Direct Compression Method

RUN	HPMC K4M	HPMC E5LV	LACTOSE	POLYOX 303	PVP	Mg. STEARATE	TALC
F_1	55	30	50	4	6	6	3
F_2	45	30	50	8	4	8	3
F_3	45	20	50	8	6	6	4
F_4	55	20	40	8	6	8	3
F_5	45	30	40	4	6	8	4
F_6	55	20	50	4	4	8	4
F_7	55	30	40	8	4	6	4
F_8	45	20	40	4	4	6	3

RESULTS AND DISCUSSIONS

Evaluation of Floating Tablet for Designed Formulations (Plackett-Burman Design)

Pre Compression Evaluation of Floating Tablet for Designed Formulations

- **Angle of Repose**

Table no.3 shows the results obtained for angle of repose for all the formulations. The values were found to be in the range of 24°.65' to 29°.65'. All the formulations showed the angle of repose within 30°, which indicates good flow for all the formulation.

- **Density**

Both loose bulk density (LBD) and tapped bulk density results are shown in Table no.3. The loose bulk density and tapped bulk density for all the formulations varied from 0.311 gm/cm3 to 0.329 gm/cm3 and 0.367 gm/cm3 to 0.394 gm/cm3 respectively. The values obtained lies within the acceptable range and no large differences found between loose bulk density and tapped bulk density. These results help in calculating the % compressibility of the powder.

- **Percentage Compressibility (Carr's Consolidation Index)**

Table no.3 shows the results obtained for percentage compressibility. The percentage compressibility of powder mix was determined by the equation given for Carr's Consolidation Index in methodology section. The percentage compressibility for all the formulations lies within the range of 12.29 to 16.79; hence they are showing good compressibility.

- **Hausner Ratio**

Table no.3 shows the results obtained for hausner ratio. The hausner ratio of powder mix was determined by the equation given in methodology section using the datas obtained for loose bulk density and tapped bulk density. The hausner ratio for all the formulations lies within the range of 1.14 to 1.20, which is nearer to optimum Hausner ratio of 1.25.

Table:-3 Pre-Compression Parameter of Powder

Sr. No	Formula	Angle of Repose	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	% Compressibility	Hausner Ratio
1	F_1	26.30	0.329	0.394	16.497	1.197
2	F_2	28.45	0.312	0.370	15.675	1.185
3	F_3	24.65	0.324	0.375	13.60	1.157
4	F_4	26.48	0.317	0.381	16.797	1.201
5	F_5	29.65	0.315	0.367	14.168	1.165
6	F_6	25.49	0.314	0.358	12.290	1.140
7	F_7	26.19	0.311	0.369	15.718	1.186
8	F_8	27.48	0.322	0.386	16.580	1.198

Post Compression Evaluation of Floating Tablet for Designed Formulations

- **Hardness**

The hardness of all the formulations was checked using Monsanto Hardness Tester, by the method described in methodology section and is reported in Table 4. The average hardness of all the batches is in the range of 2.30 to 2.60 kg/cm2. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform in

specific method and possess good mechanical strength with sufficient hardness.

- **Friability**

Friability testing of formulations was done as described in the methodology section. All tablets showed % friability below 1% and thus were in acceptable range and passed the test. The results are given in table 4

- **Weight Variation**

Twenty tablets were taken for weight variation testing. All the tablets passed the weight variation test and were in the permissible range of percentage deviation $\pm$ 7.5. The values are given in table 4

Table 4: Hardness, Friability, Weight Variation

Sr. No	Batch Code	Hardness (KG/CM^2)	Friability (%)	Weight Variation (MG)
1	F_1	2.5±0.29	0.56	200±0.15
2	F_2	2.6±0.42	0.63	200±0.26
3	F_3	2.5±0.30	0.46	200±0.25
4	F_4	2.5±0.46	0.75	200±0.19
5	F_5	2.4±0.35	0.59	200±0.09
6	F_6	2.6±0.49	0.43	200±0.24
7	F_7	2.3±0.34	0.67	200±0.27
8	F_8	2.5±0.50	0.48	200±0.18

FLOATING LAG TIME AND TOTAL FLOATING TIME

Table 5: Floating Lag Time, Total Floating Time

Sr. No.	Formulation	Lag Time (Sec)	Buoyancy Time (H)
1	F_1	129	25
2	F_2	116	24
3	F_3	188	24
4	F_4	202	24
5	F_5	232	26
6	F_6	213	27
7	F_7	156	24
8	F_8	235	26

DISSOLUTION STUDIES

In vitro drug release studies were performed as per the procedure described in methodology section. The samples were withdrawn at specified time intervals and analyzed by UV method. % cumulative drug release was calculated on the basis of mean amount of Atorvastatin present in the respective formulation. *In vitro* drug release data for formulation (F1- F4) shown in table 6, for (F5-F8) shown in table 7. The percentage cumulative drug release of formulations of Atorvastatin was plotted against time to obtain drug release profiles as shown in Figure 5.10.

Table 6: In-Vitro Drug Release

Time (Hrs)	Cumulative Drug Release (%)			
	F_1	F_2	F_3	F_4
0	0	0	0	0
1	4.69±0.56	4.83±0.17	6.74±0.76	9.38±0.85
2	11.43±0.48	8.28±0.07	17.15±0.45	18.98±0.64
3	18.77±0.16	16.57±0.45	26.10±0.04	21.71±0.92
4	23.55±0.09	18.86±0.37	38.95±0.18	31.04±0.87
5	32.95±0.07	24.08±0.19	47.93±0.47	36.06±0.45
6	39.73±0.38	33.26±0.58	51.57±0.87	44.96±0.67
7	47.61±0.35	35.72±0.47	55.59±0.26	47.65±0.38
8	50.52±0.03	42.86±0.08	69.49±0.22	51.95±0.49
9	57.10±0.77	49.06±0.70	73.53±0.37	58.09±0.08
10	61.26±0.46	52.19±0.47	82.84±0.14	60.71±0.45
11	65.51±0.08	57.89±0.87	87.62±0.77	66.86±0.55
12	69.68±0.25	60.67±0.94	92.62±0.49	72.72±0.78
24	90.12±0.22	98.73±0.62	97.66±0.55	95.95±0.23

Table 7: In-Vitro Drug Release

Time (Hrs)	Cumulative Drug Release (%)			
	F_5	F_6	F_7	F_8
0	0	0	0	0
1	3.22±0.27	11.06±0.74	13.62±0.46	14.58±0.89
2	7.18±0.48	21.48±0.93	21.84±0.22	24.63±0.45
3	14.37±0.69	24.50±0.44	25.46±0.37	34.33±0.74
4	16.36±0.47	34.13±0.62	35.08±0.44	40.15±0.85
5	21.73±0.79	37.68±0.51	41.79±0.88	44.52±0.12
6	23.95±0.34	47.61±0.47	50.62±0.07	53.14±0.45
7	30.79±0.46	55.28±0.04	54.63±0.18	59.93±0.20
8	33.24±0.52	58.35±0.88	57.26±0.68	67.25±0.79
9	41.33±0.64	62.00±0.19	65.23±0.97	71.58±0.36
10	43.94±0.81	69.17±0.63	72.48±0.45	78.69±0.37
11	49.78±0.09	72.11±0.94	77.84±0.52	82.29±0.97
12	51.67±0.18	75.48±0.41	81.07±0.15	90.22±0.64
24	80.66±0.47	94.83±0.78	96.33±0.74	97.12±17

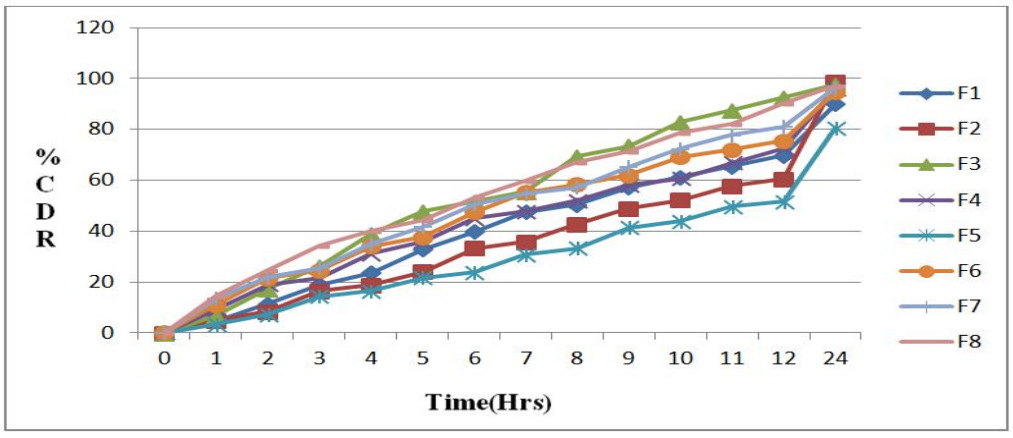

Figure 1: % in Vitro Drug Release Profile of F1 – F9 Formulation

DRUG RELEASE KINETICS OF FLOATING TABLET FOR DESIGNED FORMULATIONS

Table 8: R^2 and K Values of the Release Profiles of Designed Formulations Corresponding to Zero Order, First Order and Higuchi Kinetics

Form	Zero-order		First-order		Higuchi	
	R^2	K_0	R^2	K_1	R^2	Kh
F_1	0.8053	5.028	0.9837	0.089	0.9077	17.701
F_2	0.9577	4.696	0.9547	0.073	0.8593	16.001
F_3	0.6021	6.263	0.9608	0.140	0.8930	22.585
F_4	0.7817	5.283	0.9912	0.097	0.9508	18.722
F_5	0.9484	3.895	0.9782	0.057	0.8596	13.293
F_6	0.6739	5.560	0.9935	0.110	0.9535	19.943
F_7	0.6426	5.775	0.9875	0.119	0.9479	20.770
F_8	0.5163	6.180	0.9849	0.140	0.9401	22.475

Table 9: R^2, n and Kkp Values of the Release Profiles of Designed Formulations Corresponding to Korsmeyer-Peppas Models

Formulation	Korsmeyer-Peppas		
	R^2	Kkp	N
F_1	0.9515	12.002	0.667
F_2	0.9860	7.315	0.832
F_3	0.9007	19.499	0.564
F_4	0.9793	13.880	0.629
F_5	0.9807	6.229	0.821
F_6	0.9639	16.820	0.574
F_7	0.9554	18.005	0.562
F_8	0.9405	21.784	0.514

Dissolution profiles were fitted to various model and release data were analyzed on the basis of Korsmeyer-Peppas equation, First order, Zero order, Higuchi kinetics. From the Korsmeyer-Peppas equation, the diffusion exponent ranges from 0.514 to 0.832. From the result, All the batches exhibited non-Fickian. The R^2 values are given in above table. Drug release mechanisms followed First order and Korsmeyer-Peppas model.

SIMILARITY FACTOR (f_2)

Table 10: Similarity Factor

Similarity Factor f_2	Mean R Vs Individual T		Mean R Vs Mean T
	Mean	SE	
	13.69		13.69

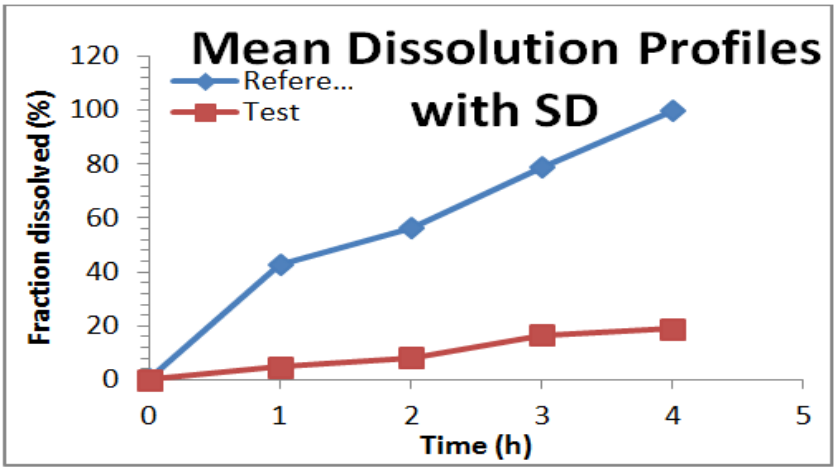

Figure 2: Mean Dissolution Profile with SD

COMPARISON WITH MARKETED PRODUCT

- Conventional tablets are taken for comparison. In vitro dissolution of the tablet was done and it is compare with the optimized formulation (F_2).
- Brand name: Lipitor
- Company name: pfizer Pharmaceuticals Limited
- Labelled claim: 80 mg Atorvastatin calcium

Table 11: In vitro drug release of batch F_2 and marketed product

Time (hrs)	% Cumulative Drug Release	
	F_2	Marketed Product
0	0	0
1	4.83±0.17	42.64±0.38
2	8.28±0.07	56.48±0.45
3	16.57±0.45	78.72±0.08
4	18.86±0.37	99.83±0.15
5	24.08±0.19	-
6	33.26±0.58	-
7	35.72±0.47	-
8	42.86±0.08	-
9	49.06±0.70	-
10	52.19±0.47	-
11	57.89±0.87	-
12	60.67±0.94	-
24	98.73±0.62	-

Note: Values are mean value of 3 observation (N=3), and values in parenthesis are standard deviation (± SD)

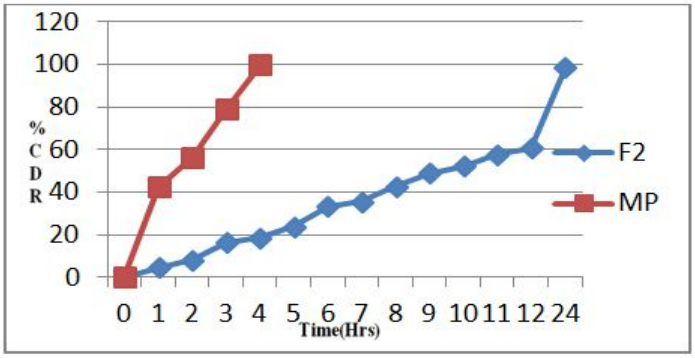

Figure 3: Comparison of In-vitro Drug Release of Marketed Product of Atorvastatin Calcium with Formulation F_2

From the Figure 5.11, it can be concluded that formulation 'F_2' has shown 98.97±0.62% drug release within 24 hrs while marketed product shows about 99.83±0.15% drug release within 4 hrs. The results indicate that the prepared tablets could improve bioavailability.

STABILITY STUDY OF OPTIMIZED FORMULATION

Stability study was carried out at 40°C and 75 % RH and at room temperature for one month storage. Batch F_2 was taken for stability study. Various parameters were compared for stability study.

Table 12: Comparison of Various Parameters for Stability Study

Evaluation Parameter	Before One Month	After One month	
		Accelerated	Room Temp.
Hardness	2.6±0.42	2.6± 0.20	2.5 ± 0.40
Percentage Friability	0.63	0.60	0.55
Lag Time (sec)	116	118	114

Table 13: Comparison of Drug Release Profile of Batch F_2

Time (min)	Before One Month	After One Month	
		Accelerated	Room Temp.
0	0	0	0
1	4.83±0.17	2.25±0.23	3.45±0.04
2	8.28±0.07	6.86±0.48	7.69±0.47
3	16.57±0.45	15.36±0.79	16.67±0.26
4	18.86±0.37	16.78±0.12	17.74±0.35
5	24.08±0.19	22.61±0.06	23.32±0.78
6	33.26±0.58	31.48±0.38	32.84±0.98
7	35.72±0.47	33.97±0.48	34.65±0.45
8	42.86±0.08	40.64±0.06	41.12±0.15
9	49.06±0.70	47.87±0.79	48.18±0.23
10	52.19±0.47	50.89±0.89	51.28±0.04
11	57.89±0.87	55.12±0.69	56.73±0.75
12	60.67±0.94	58.32±0.35	59.30±0.15
24	98.73±0.62	96.23±0.75	97.23±0.48

Note: Values are mean value of 3 observation (N=3), and values in parenthesis are standard deviation (± SD)

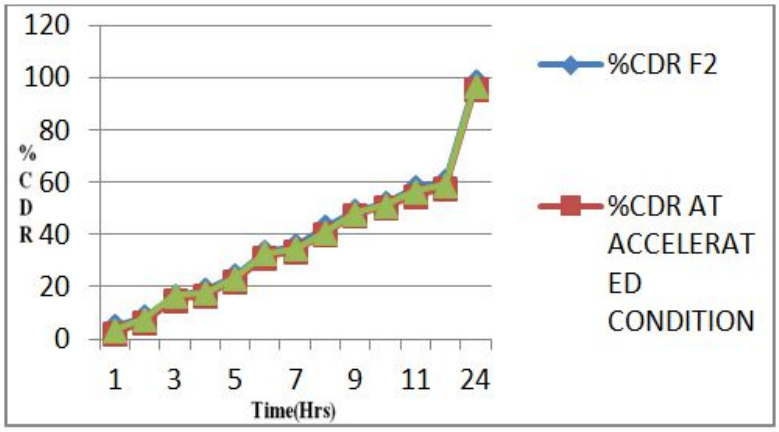

Figure 4: Comparison of Stability Data (Formulation F2, Formulation Stored at Room Temp. & Accelerated Condition)

CONCLUSIONS

The non-effervescent floating tablets of atorvastatin calcium was satisfactorily formed with appropriate physical characteristic.

Literature survey was carried out for selection of suitable excipients. The drug and excipients compatibility study was conducted to determine and select bland excipients for formulation.

Non-Effervescent floating tablets were formulated using diluents like Lactose and different polymers like HPMC K4M and HPMC E5LV.

Plackett-Burman Design was applied by using two polymers as an independent factor to observe the effect of polymers in combination. Tablets were prepared. The tablets were evaluated for Lag time, Weight variation, Hardness, Percentage friability, Total floating time. Batch F2 was optimized by in-vitro drug release 99.74%, Lag time 116 seconds and Total floating time 24 Hours. There were no significant differences between experimental and predicted values.

Formulation F2 contains HPMC K4M and HPMC E5LV. Formulation F2 was subjected to further Stability study. Stability study was carried out at 45oC and 75 % RH according to the ICH guidelines. The samples were analyzed at intervals of first month for the dissolution profile and lag time. The results indicated that there was no significant variation in the formulations. These results revealed that the Non-effervescent floating tablets had better absorption, when compared to oral tablets of Atorvastatin calcium.

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